

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A tumor necrosis factor mutant protein specific to either TNF-R1 or TNF-R2, where one or more amino acid residues selected from the group consisting of the 29th, 31st, 32nd, 84th to 89th, 145th, 146th and 147th amino acid residues, ~~or the group consisting of the 84th to 89th amino acid residues from the N terminal~~ of the amino acid sequence of SEQ ID NO:1 are replaced with other amino acid(s).

2. (Currently amended) The tumor necrosis factor mutant protein of claim 1, ~~which has an antagonistic activity against tumor necrosis factor,~~

where the 29th amino acid residue ~~from the N terminal~~ of the amino acid sequence of SEQ ID NO:1 is replaced with arginine, histidine or serine; the 31st amino acid residue replaced with arginine, asparagine, glutamic acid, proline or serine; the 32nd amino acid residue replaced with histidine, methionine, threonine or tyrosine; the 145th amino acid residue replaced with alanine, asparagine, aspartic acid or serine; the 146th amino acid residue replaced with

In re of: MAYUMI4

asparagine, glycine, methionine or serine; and the 147th amino acid residue replaced with alanine, asparagine, proline, threonine or a stop codon;

where the 145th amino acid residue is replaced with alanine, lysine or arginine; the 146th amino acid residue replaced with glutamic acid, asparagine, aspartic acid or threonine; and the 147th amino acid residue replaced with threonine or aspartic acid; or

where the 84th amino acid residue is replaced with alanine, threonine, serine or glycine; the 85th amino acid residue replaced with proline, threonine or glycine; the 86th amino acid residue replaced with alanine, glycine, threonine or proline; the 87th amino acid residue replaced with tyrosine, isoleucine or histidine; the 88th amino acid residue replaced with glutamine, asparagine or serine; and the 89th amino acid residue replaced with arginine, histidine or glutamine.

3. (Currently amended) The tumor necrosis factor mutant protein of claim 1, ~~which has an agonist activity against tumor necrosis factor,~~ where the 29th amino acid residue ~~from the N-terminal~~ of the amino acid sequence of SEQ ID NO:1 is replaced with leucine, glutamine, threonine or lysine; the 31st amino acid residue replaced with arginine,

In re of: MAYUMI4

glycine, serine or alanine; the 32nd amino acid residue replaced with tryptophan, tyrosine, aspartic acid or glycine; the 146th amino acid residue replaced with glutamic acid, alanine or serine; and the 147th amino acid residue replaced with serine, arginine or threonine; or

where the 84th amino acid residue is replaced with threonine, serine or asparagine; the 85th amino acid residue replaced with serine, lysine, proline, tyrosine, arginine, threonine, histidine, glutamic acid, aspartic acid or alanine; the 86th amino acid residue replaced with histidine, threonine, leucine, asparagine, alanine, valine, lysine, serine, glutamine, glycine, arginine or aspartic acid; the 88th amino acid residue replaced with serine, proline, threonine, asparagine, alanine, glycine, arginine or glutamine; and the 89th amino acid residue replaced with aspartic acid, histidine, lysine, glycine, serine, proline, alanine, glutamine, phenylalanine or arginine.

4. (Currently amended) The tumor necrosis factor mutant protein of claim 21, which has an antagonistic activity against tumor necrosis factor, and ~~which is a protein comprising~~ comprises an amino acid sequence selected from the group consisting of SEQ ID NOs:9 to 22, or optionally where one or more amino acid residues selected from the group

consisting of the 11th, 65th, 90th, 98th, 112th and 128th amino acid residues ~~from the N-terminal~~ of said amino acid sequence are replaced with lysine residues ~~, and having an antagonistic activity against tumor necrosis factor.~~

5. (Currently amended) The tumor necrosis factor mutant protein of claim 31, which has an agonistic activity against tumor necrosis factor ~~which is a protein comprising and comprises~~ an amino acid sequence selected from SEQ ID NOs:37 to 59 or optionally where one or more amino acid residues selected from the group consisting of the 11th, 65th, 90th, 98th, 112th and 128th amino acid residues ~~from the N-terminal~~ of said amino acid sequence are replaced with lysine residues ~~, and having an agonistic activity against tumor necrosis factor.~~

6. (Original) The tumor necrosis factor mutant protein of claim 1, which conjugates with a water-soluble polymer.

7. (Canceled)

8. (Original) A tumor necrosis factor inhibitor, which comprises the tumor necrosis factor mutant protein of

claim 2.

9. (Original) A tumor necrosis factor preparation, which comprises the tumor necrosis factor mutant protein of claim 3.

10. (New) A method for treating or preventing diseases caused or accompanied by overexpression of endogeneous tumor necrosis factor or excessive administration of tumor necrosis factor, which comprises a step of administration of the tumor necrosis factor mutant protein of claim 4.

11. (New) A method for treating or preventing diseases effectively treated by tumor necrosis factor, which comprises a step of administration of the tumor necrosis factor mutant protein of claim 5.